

An aerial photograph of a large crowd of people on a white surface, arranged to form the geographical outline of Mexico. The people are wearing various colorful clothing, creating a vibrant, multi-colored map. The background is a plain white surface with some scattered individuals.

The logo for TECAN, featuring a stylized orange circle with a white dot inside, followed by the word "TECAN." in a bold, black, serif font, and a solid orange circle at the end.



Automated production of spheroids by magnetic cell assembly for drug response profiling

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Application Specialist Cellomics

27.02.2023





3D cell models in drug development

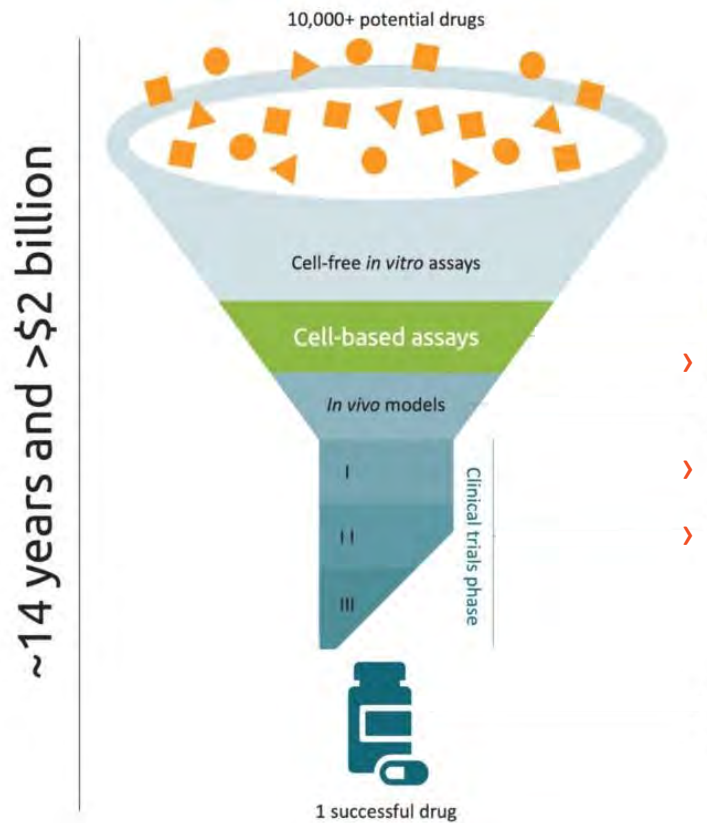
Magnetic 3D bioprinting

Manufacture 3D spheroids : From benchtop to automated solution

Key take-home messages



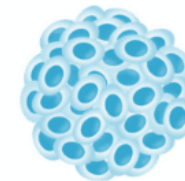
Importance of 3D cell models for drug development



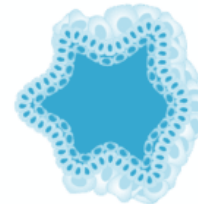
- > **<10%** of the anticancer **drugs** that enter the clinical trials **reach the market**
- > **Inefficient** preclinical models
- > **Low predictiveness** and high failure rates as a major cost driver



.. **advanced 3D cell models**
-> reduce the overall R&D cost



spheroids



organoids

Consistency

Scalability

Reproducibility

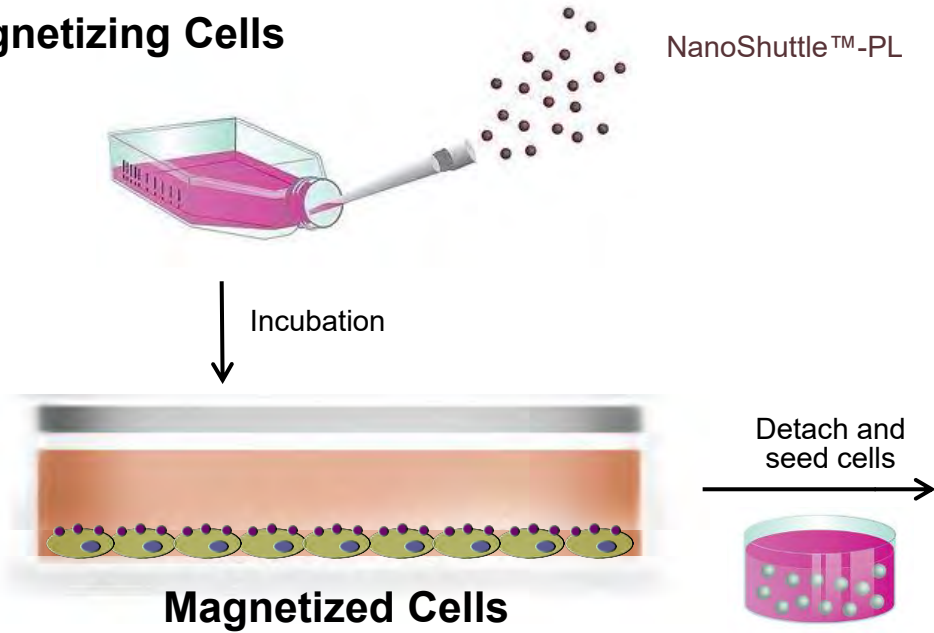
Figure adapted from [Nanolive](#)



Magnetic 3D Bioprinting



Magnetizing Cells

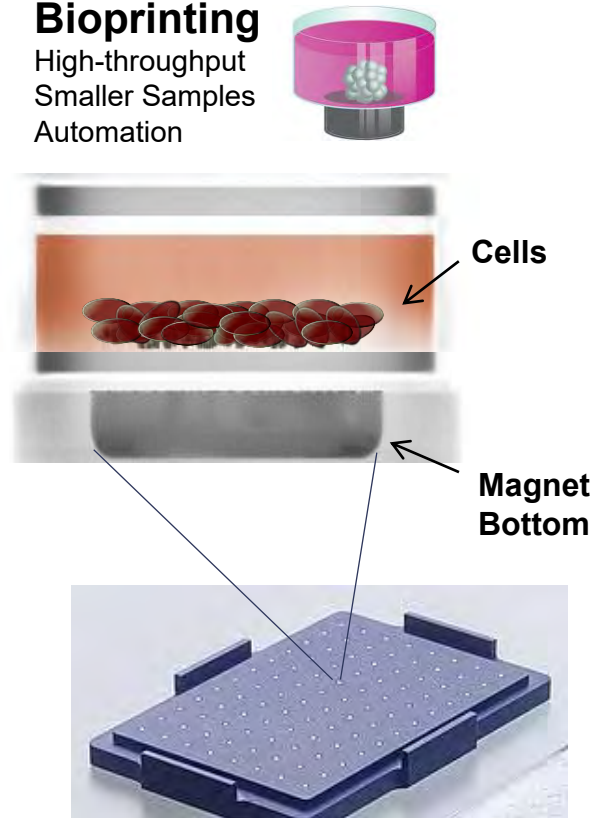


NanoShuttle™-PL

Detach and seed cells

Bioprinting

High-throughput
Smaller Samples
Automation



Cells

Magnet Bottom

Incubation

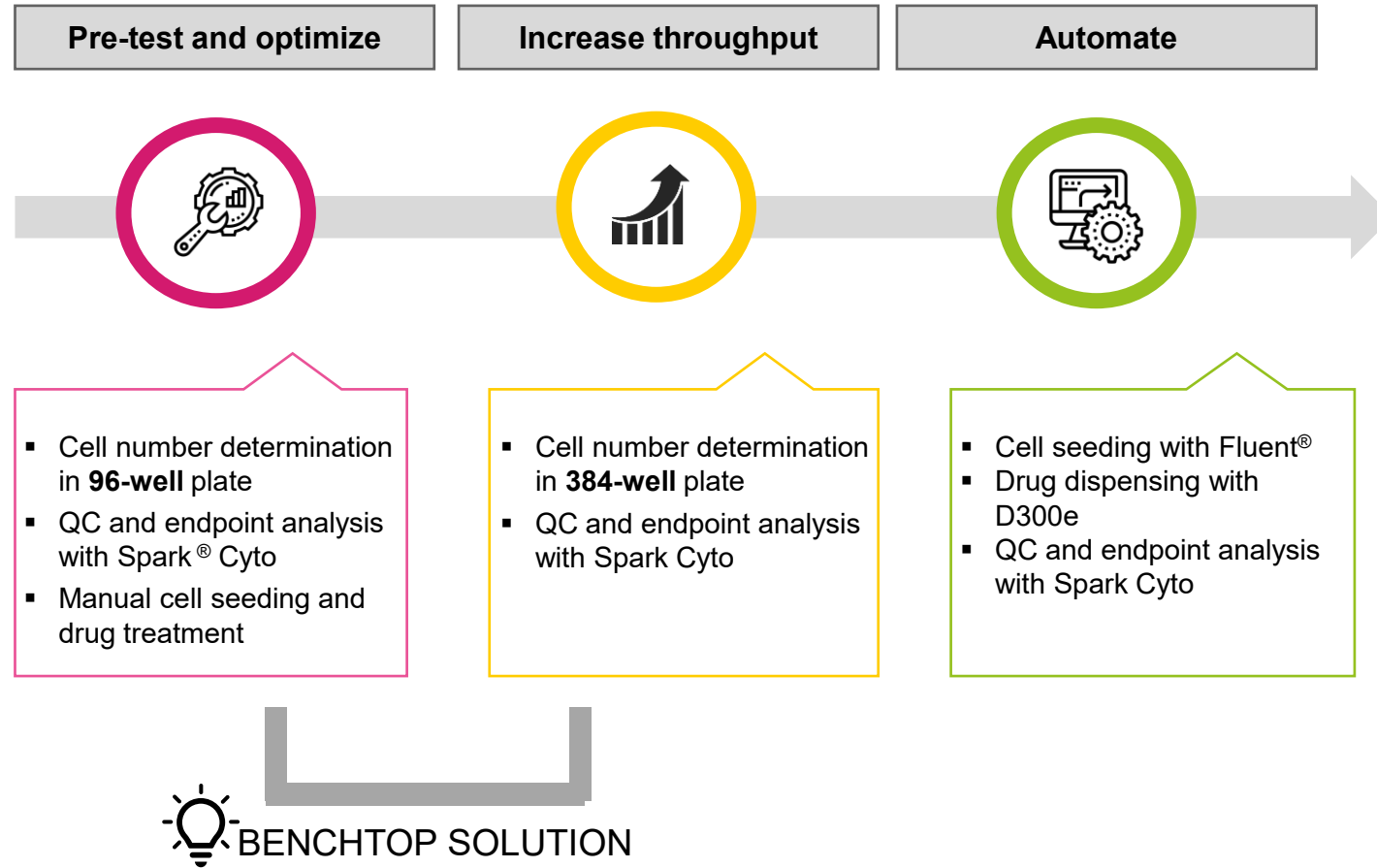


Souza et al. *Nature Nanotechnology*, April 2010
Timm et al. *Scientific Reports*, October 2013



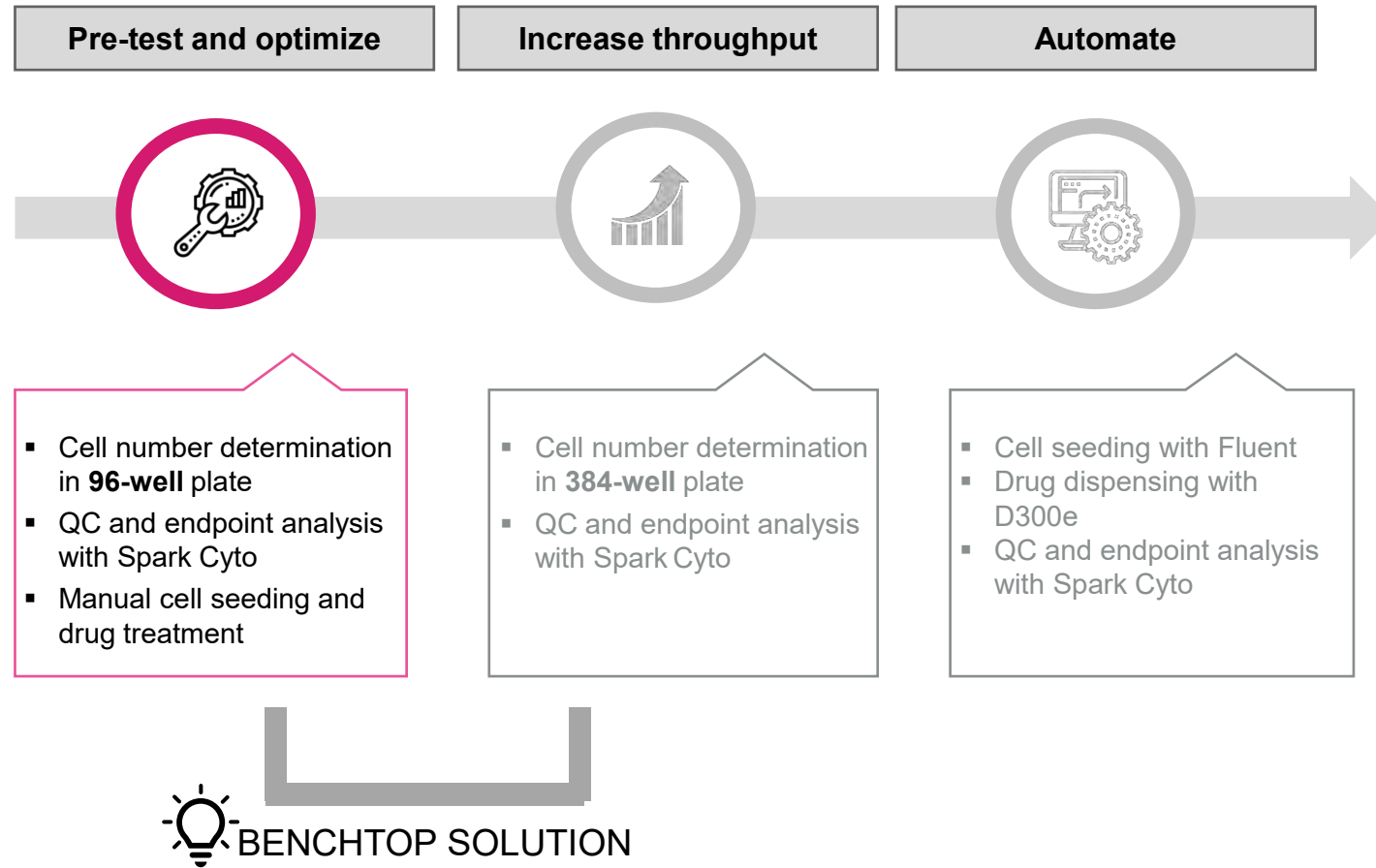
Steps in 3D cell model generation for drug testing

.. from benchtop solution to an automated workflow



Steps in 3D cell model generation for drug testing

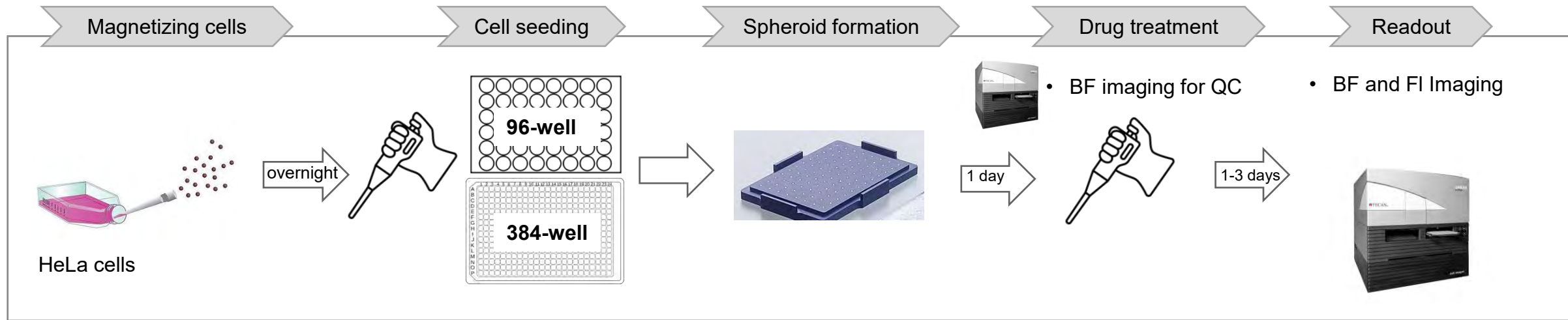
.. from benchtop solution to an automated workflow





Workflow to generate spheroids in flat bottom plates

.. in a benchtop solution

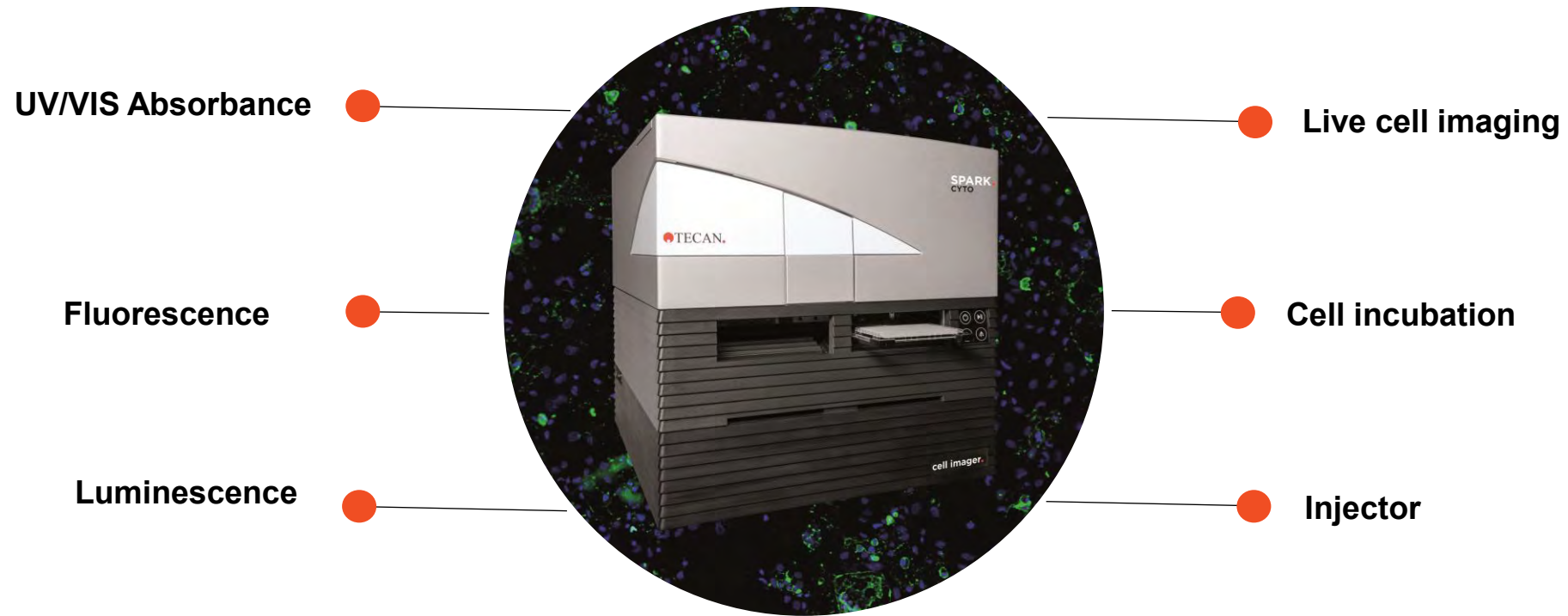


... 4-6 days from magnetization to readout



Spark Cyto is a powerful tool for multiplexing

.. combine Multi-mode reader capabilities with brightfield and fluorescence imaging



Spark Cyto is for Research Use Only. Not for use in diagnostic procedures.





Pre-testing and optimization phase requires quality control

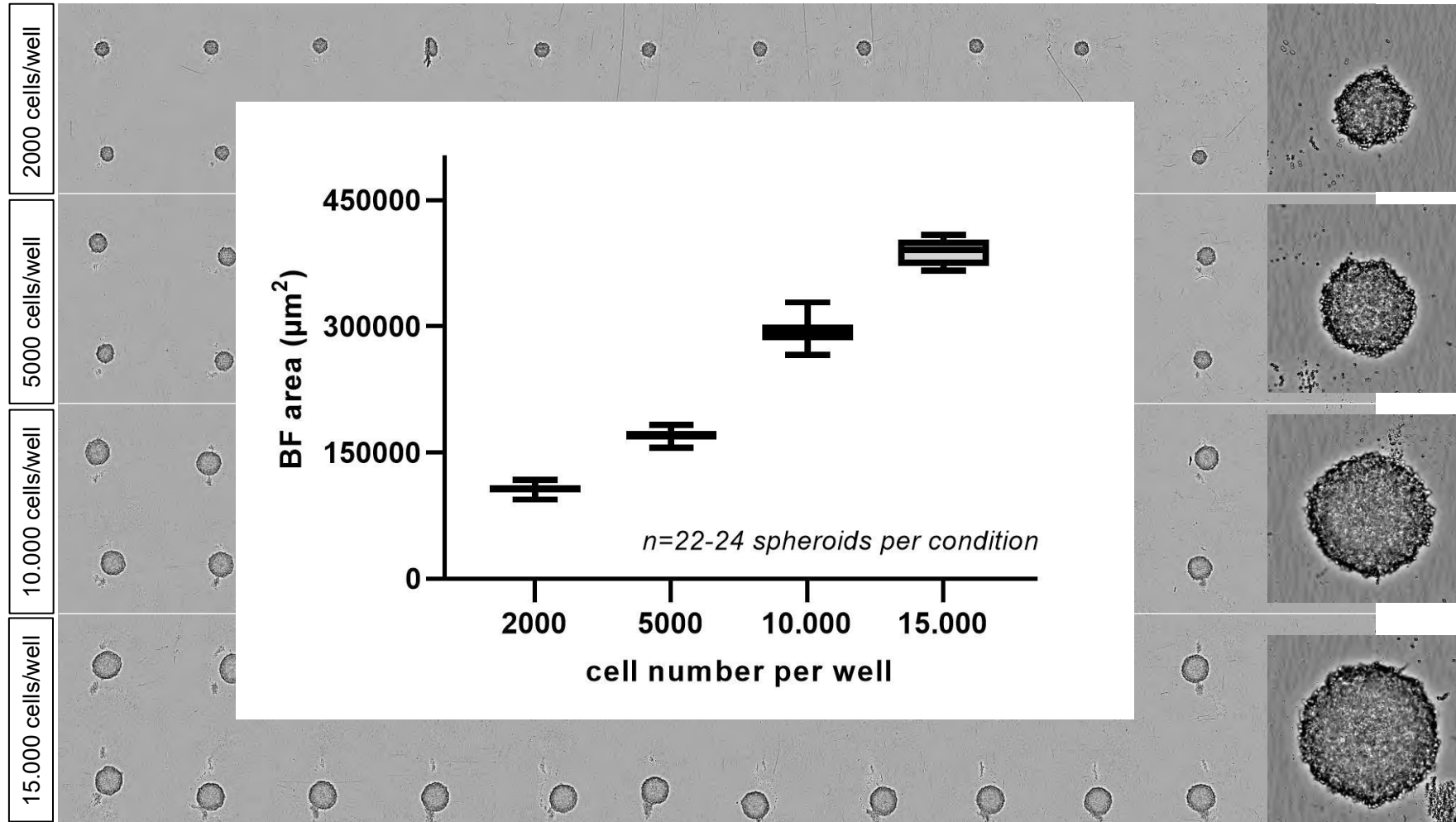


HeLa cells in a 96-well plate
4x objective
Single FOV
24 hours post seeding





Pre-testing and optimization phase requires quality control

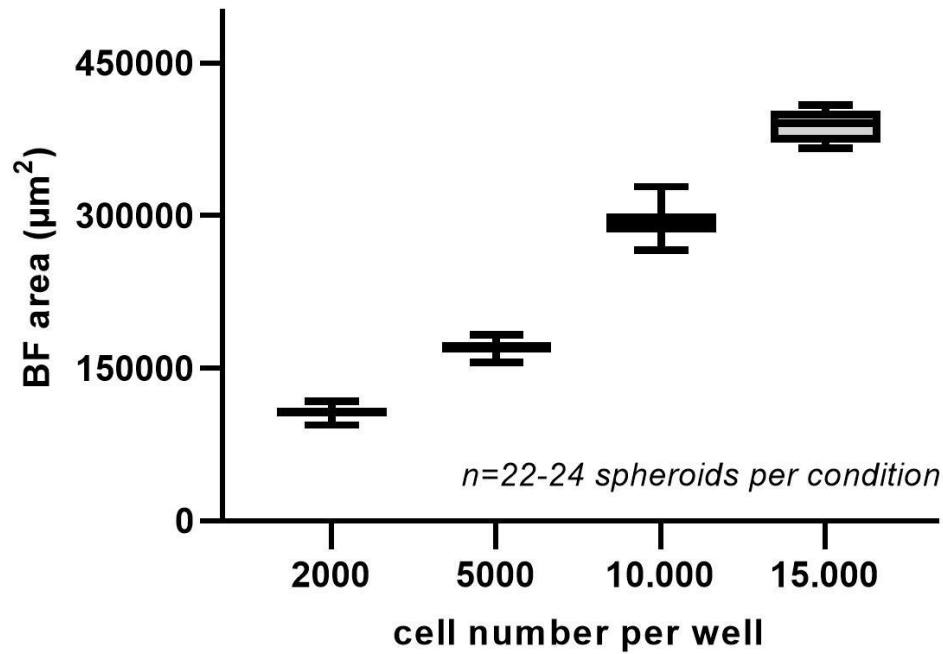


HeLa cells in a 96-well plate
4x objective
Single FOV
24 hours post seeding





Pre-testing and optimization phase requires quality control



Generation of **uniformly sized** spheroids within 24 hours with M3D bioprinting

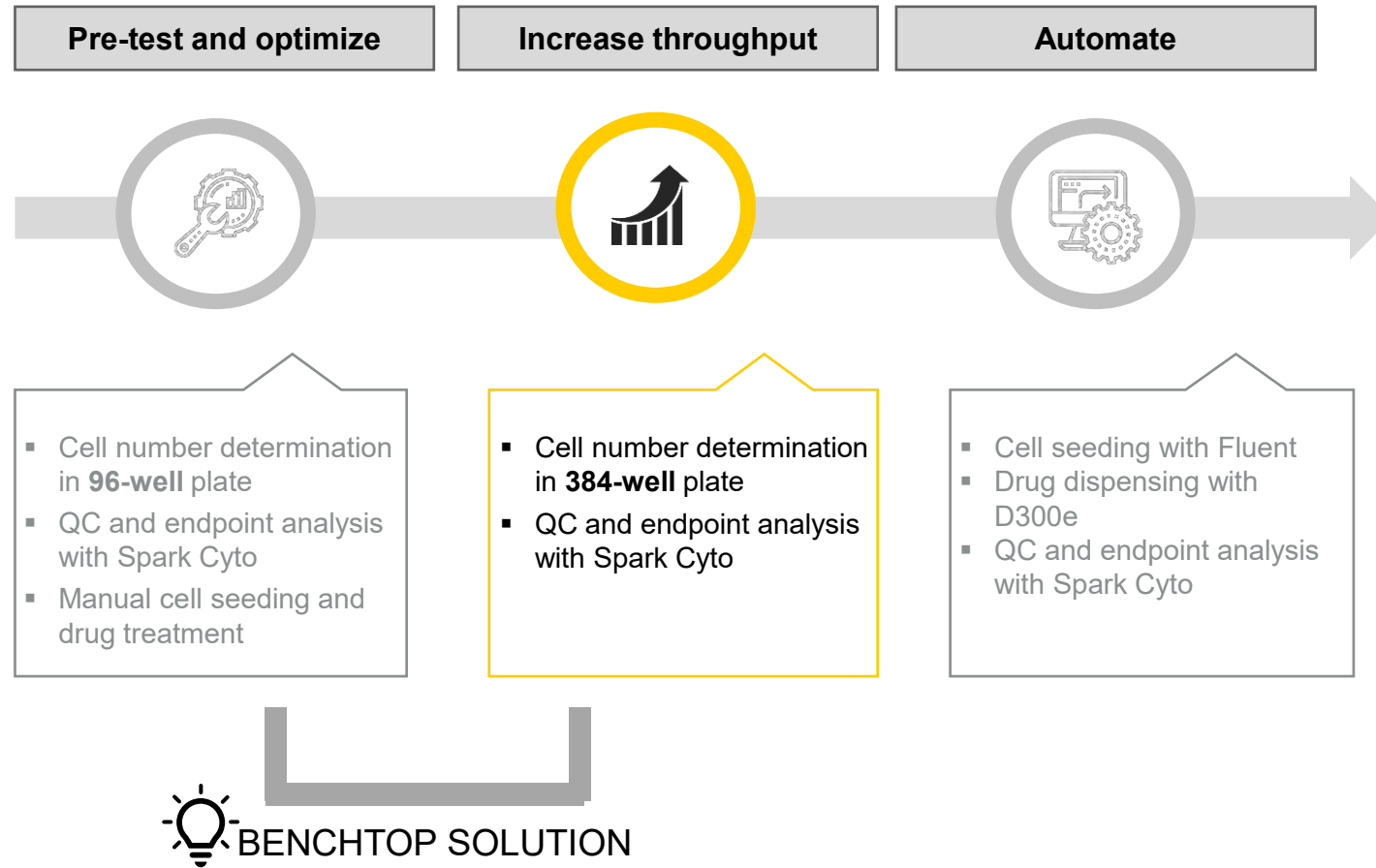


Image based **quality control** in a controlled environment confirms homogeneous spheroids



Steps in 3D cell model generation for drug testing

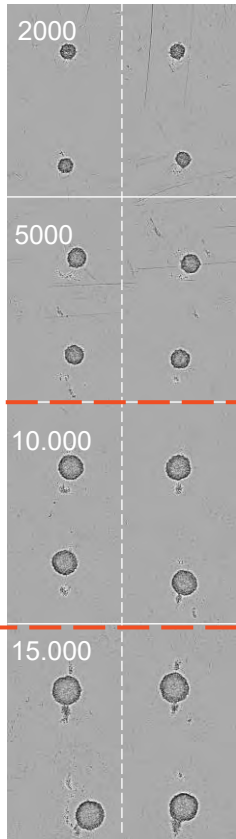
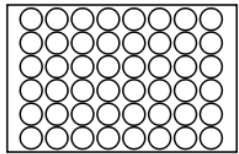
.. from benchtop solution to an automated workflow





Increase throughput through miniaturization

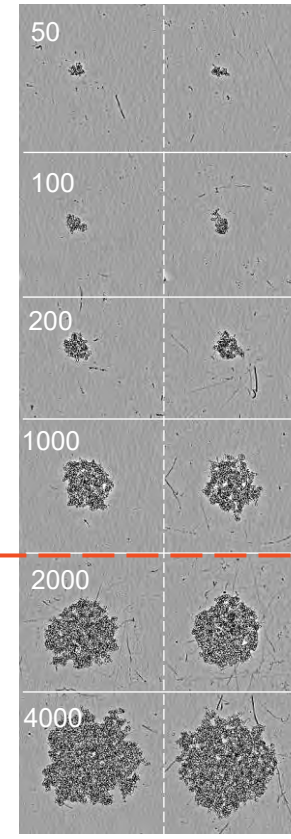
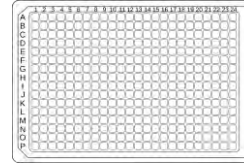
96-well plate



*HeLa cells in a
4x objective
Single FOV
24 hours post seeding*



384-well plate



*A549 cells in a 384-well plate
10x objective
Single FOV
24 hours post seeding*

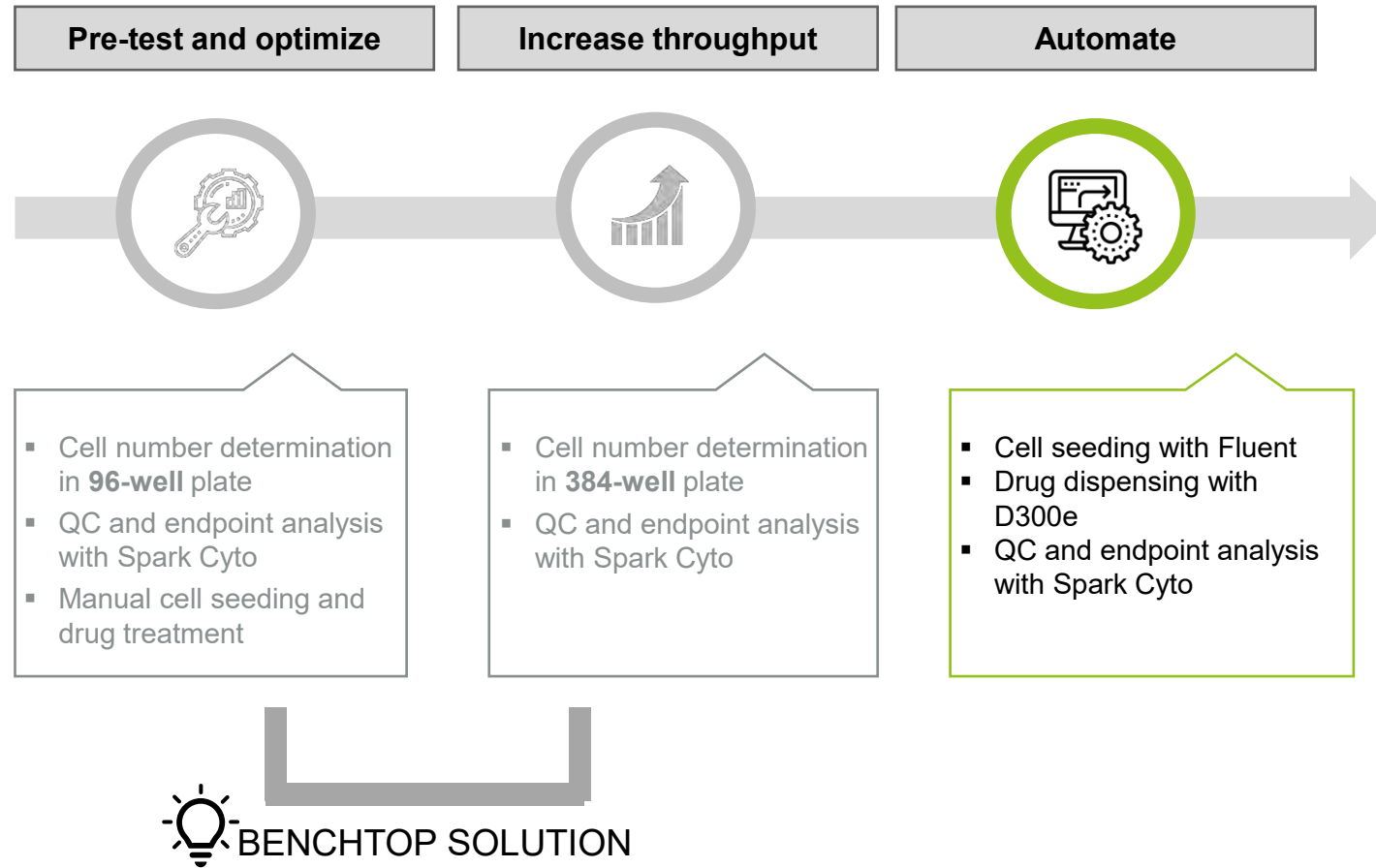


Use for automation!



Steps in 3D model generation for drug testing

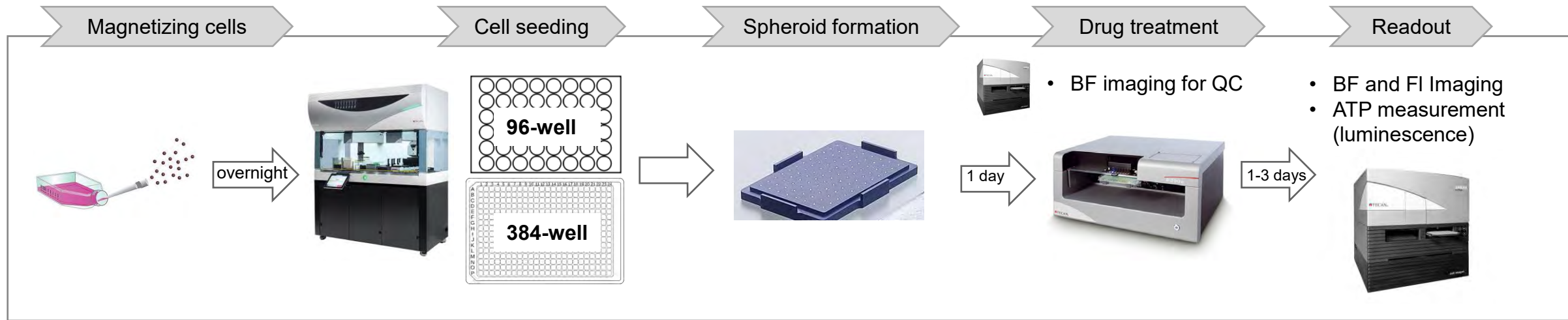
.. from benchtop solution to an automated workflow





Workflow to generate spheroids in flat bottom plates

.. in an automated way



... 4-6 days from magnetization to readout





The Fluent Automation Workstation

1 Sterile environment

Prevent cell culture contamination with HEPA hood or biosafety cabinet

2 Environmental control

Enable optimal cell viability and minimize assay variation with integrated automated incubators with environmental control

3 Monitor cell growth and health

Monitor cellular health and benefit from multiplexed analysis with Spark Cyto's imaging capabilities



4 Handle plate and tubes on deck

Fluent Finger Exchange System enables handling of both tubes and microplates with the Robotic Gripper Arm.

5 Feed and passage cells

Automate routine cell culture work such as cell seeding, medium exchange and cell harvesting on Tecan liquid handling platforms.

6 Integrate 3rd party devices

Integrate centrifuges, incubators, or cell imaging systems with Tecan Labwerx to automate the complete workflow.





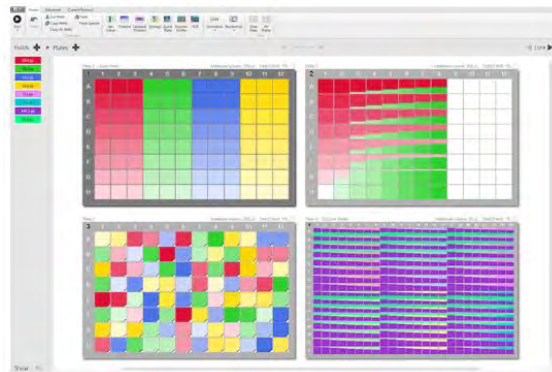
The Tecan D300e Digital Dispenser



T8+ cassette



D4+ cassette



A complete package

● D300e digital dispenser

● Ready-to-use cassettes

● Powerful and easy-to-use software



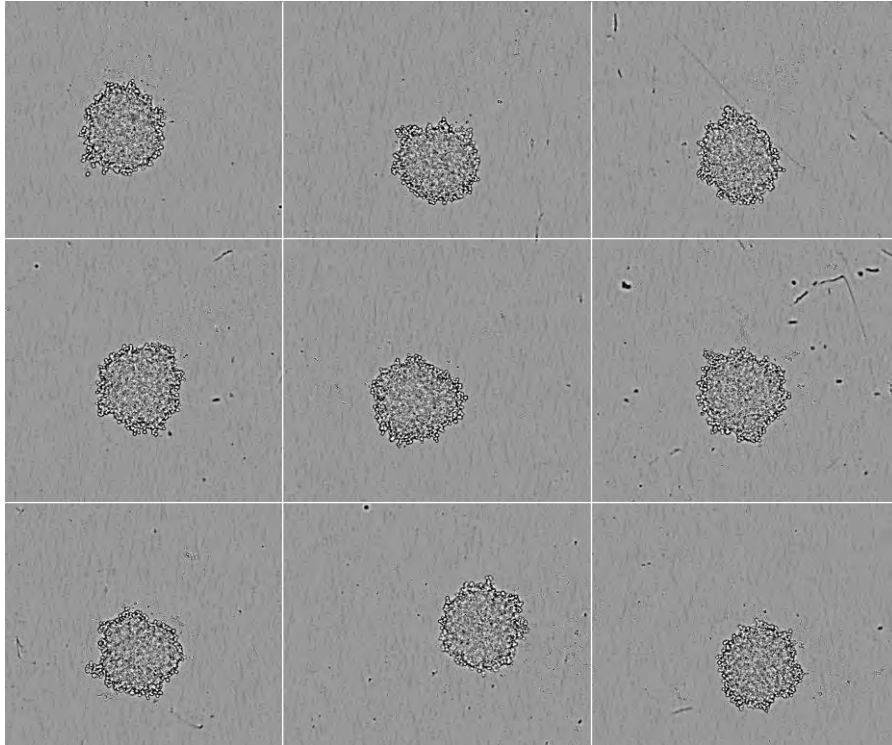
- + from pL to μ L scale
- + direct sample addition from stock solutions
- + small footprint
- + time saving
- + compound saving
- + DMSO and aqueous dispensing
- + supports 12- to 1536- well plates
- + randomized dispensing, reduce edge effects

Tecan D300e is for Research Use Only. Not for use in diagnostic procedures. Tecan D300e Digital Dispenser is a product of HP Inc. CA, USA.



Rapid dispensing of drugs ensures consistency and reliability

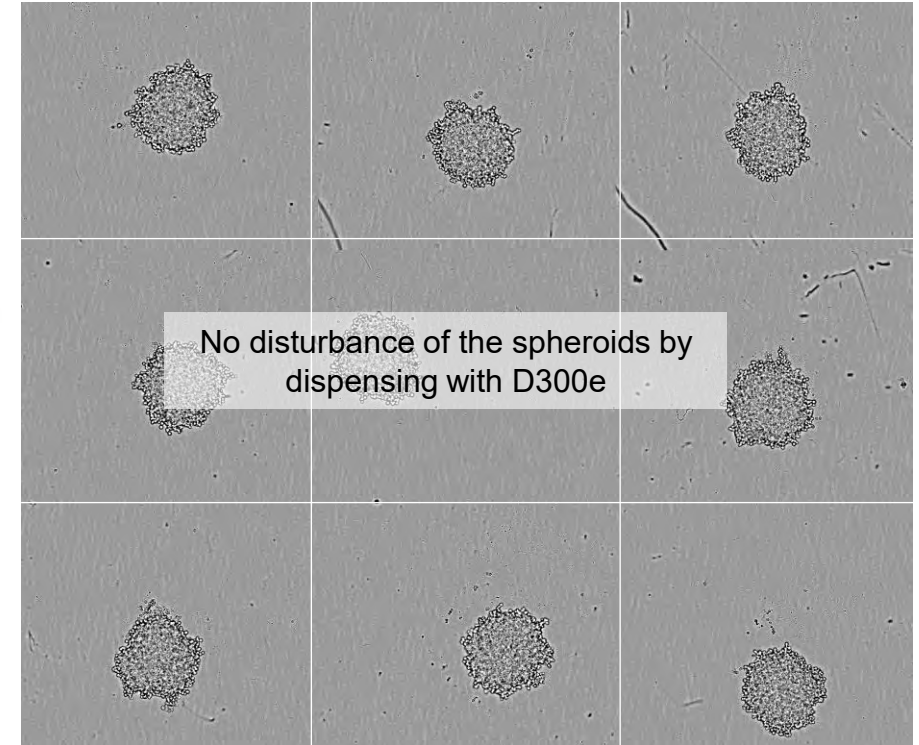
Before dispensing



D300e Digital Dispenser



After dispensing



Example images of HeLa spheroids (cutouts)





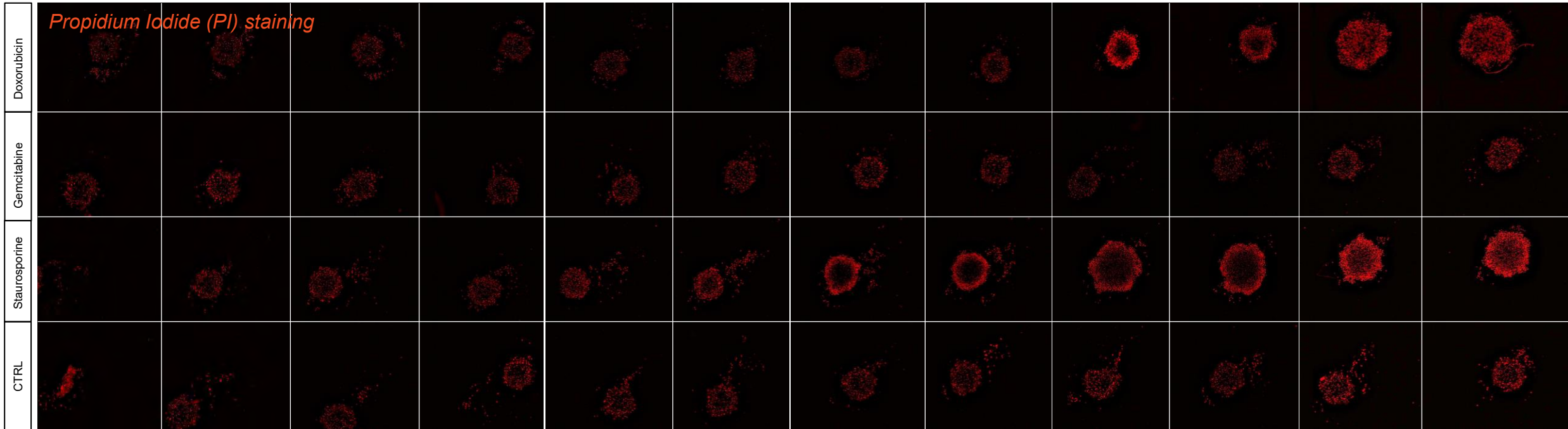
Importance of imaging based multiplexing



HeLa cells
10x objective
Single FOV
24 hours post treatment



	0.01 μ M	0.04 μ M	0.16 μ M	0.63 μ M	2.50 μ M	10 μ M
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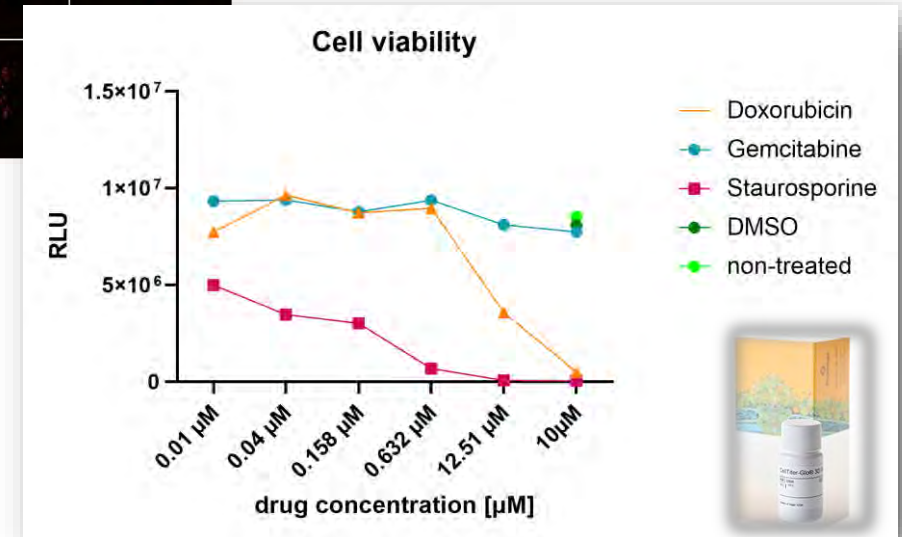
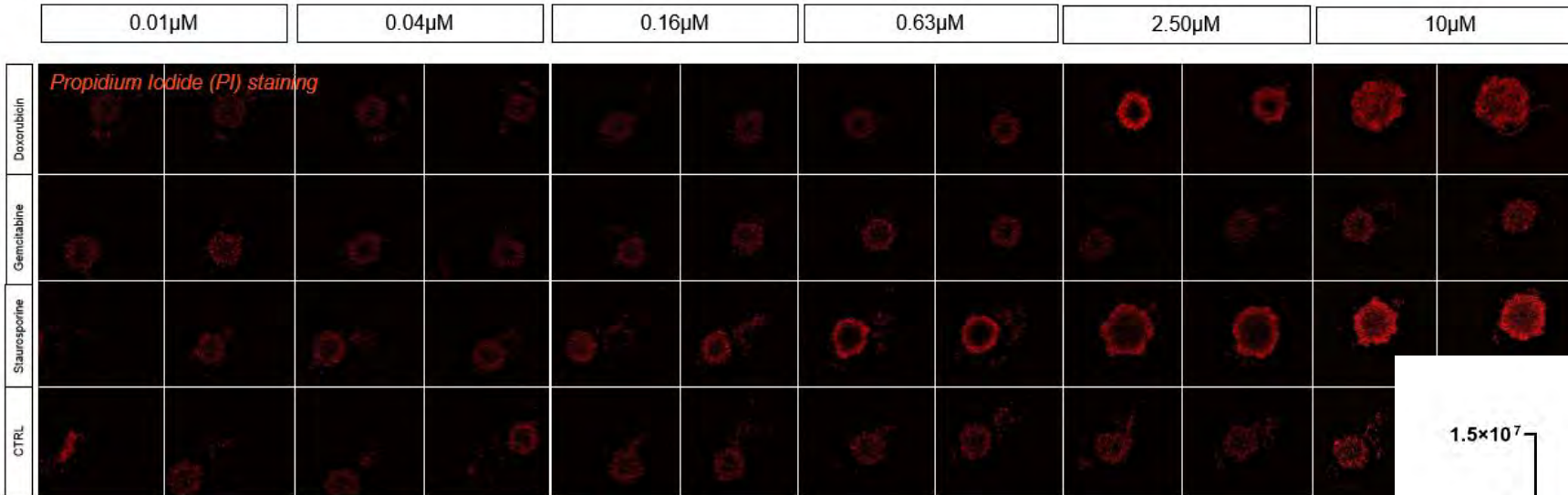




Importance of imaging based multiplexing



HeLa cells
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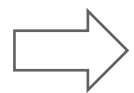
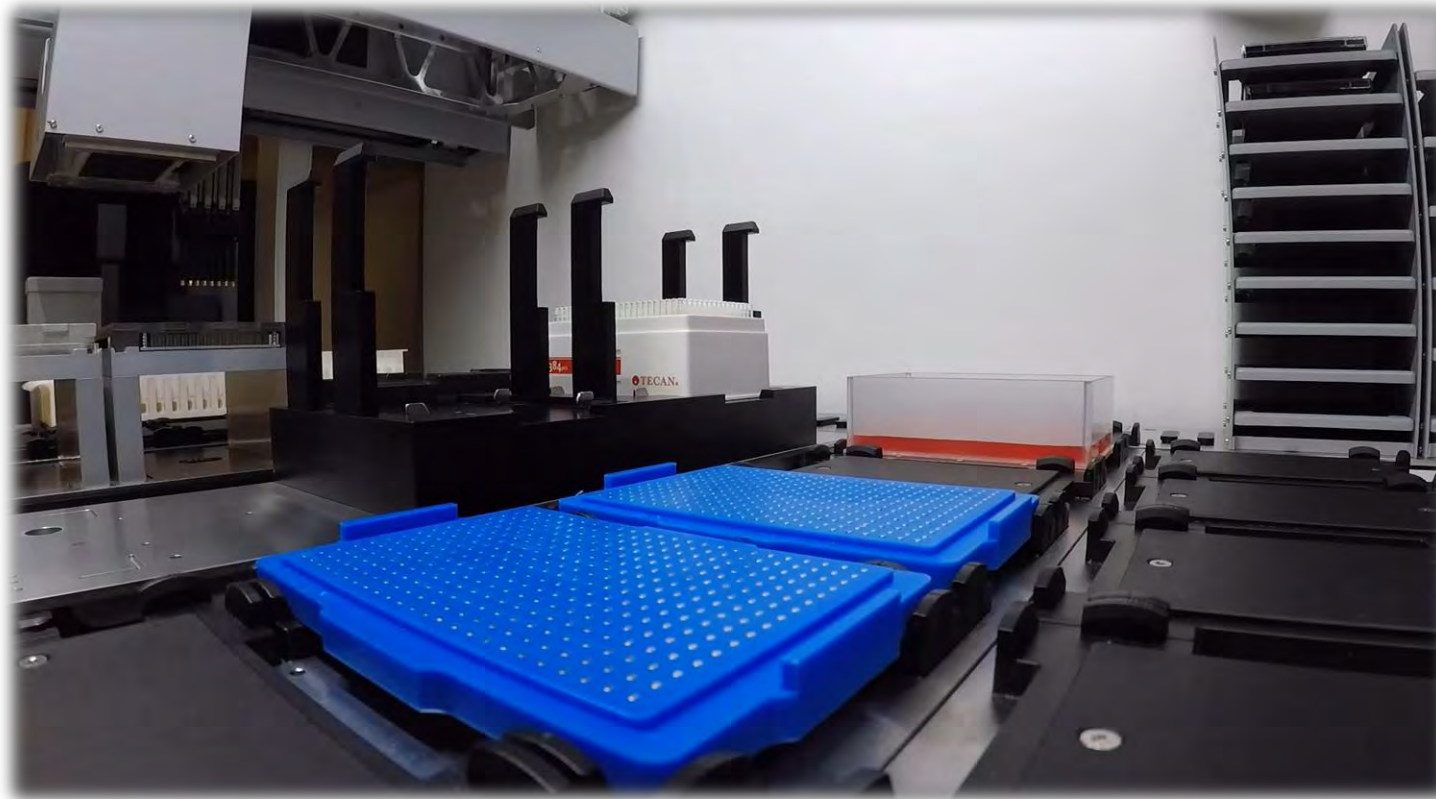


➡ Inverse correlation between dead cell staining (PI) and ATP viability assay

➡ Multiplexing to further support meaningfulness of obtained results



Cell seeding and plate transfers with the Fluent



fully automated cell distribution and plate incubation for spheroid generation via magnetic 3D bioprinting





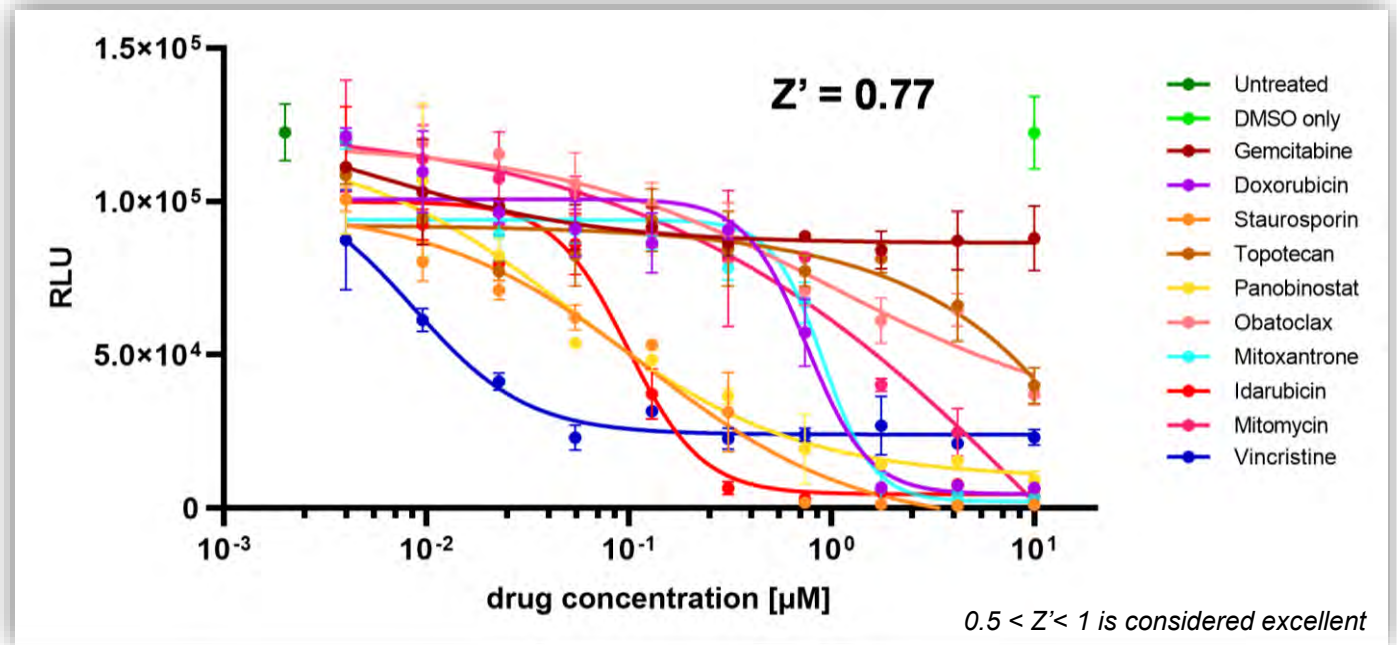
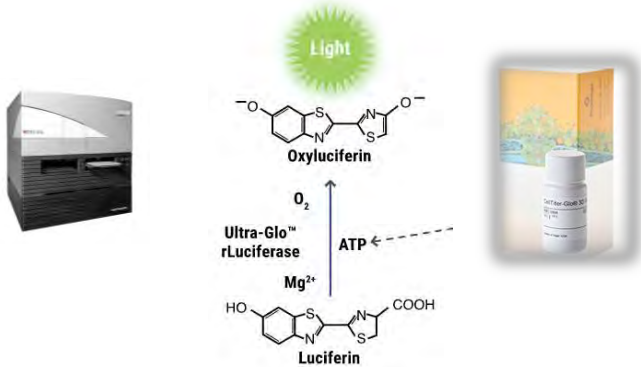
Drug response profiling with HeLa spheroids

Drug dispensing



72hrs

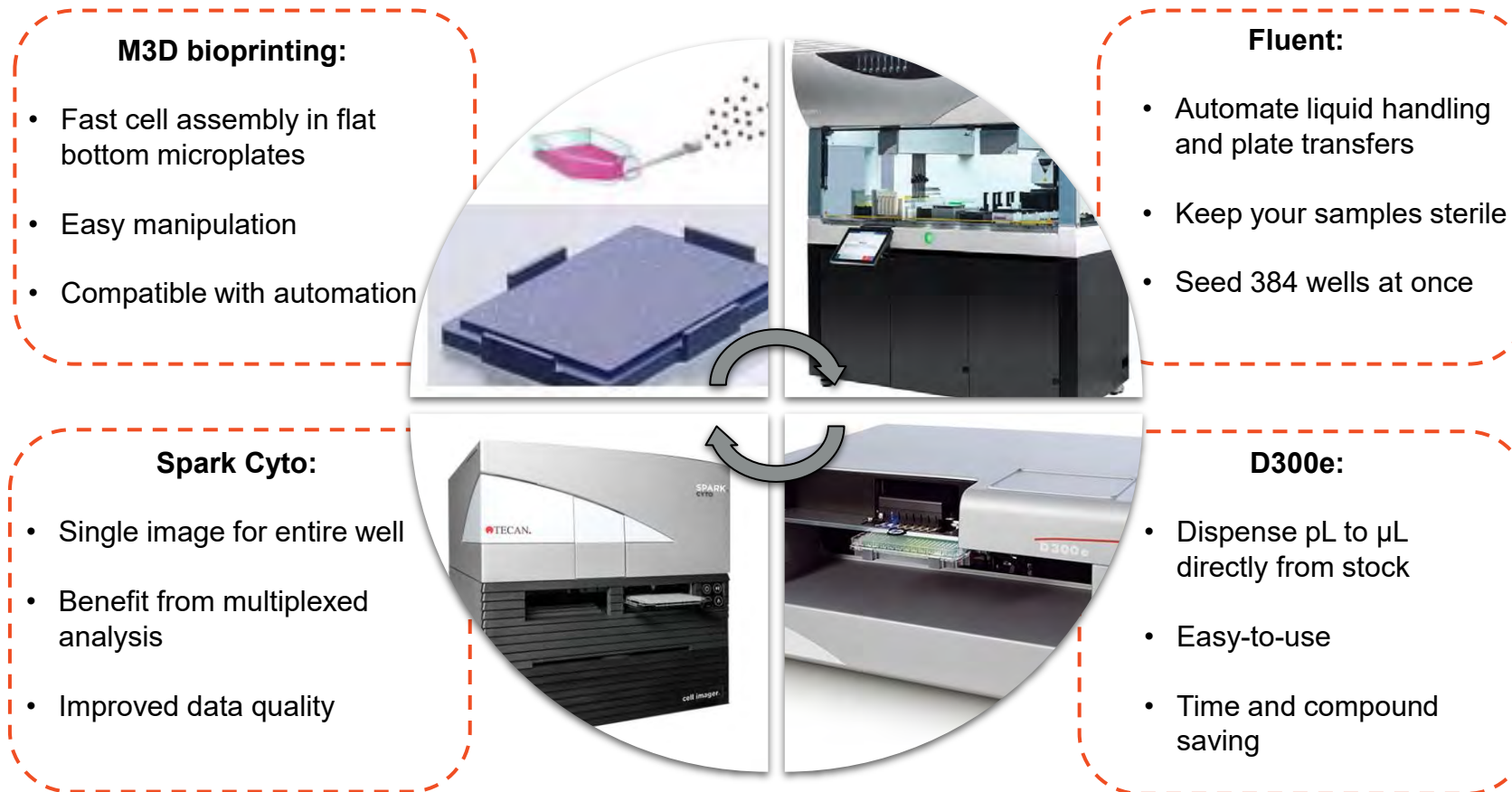
CellTiter-Glo® 3D viability assay



Drug	Gemcitabine	Doxorubicin	Staurosporine	Topotecan	Panobinostat	Obatoclox	Mitoxantrone	Idarubicin	Mitomycin	Vincristine
IC50 [μM]	na	0.78	0.11	na	0.06	2.42	0.92	0.10	0.92	0.01
R ²	na	0.94	0.96	0.74	0.94	0.92	0.93	0.95	0.94	0.93

Summary

... complete drug screening workflow automation with Tecan's equipment using M3D bioprinting approach



Acknowledgements



- Magdalena Eckschlager
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für Angewandte Wissenschaften



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- Ina Albert
- Britta Striegl

תודה
Dankie Gracias
Спасибо شكراً
Köszönjük Merci Takk
Grazie Dziękujemy Děkojame
Terima kasih
Ďakujeme Vielen Dank Paldies
Kiitos Täname teid 谢谢
Thank You Tak
感謝您 Obrigado Teşekkür Ederiz
Σας Ευχαριστούμ 감사합니다
Бодхон
Bedankt Děkujeme vám
ありがとうございます
Tack



- Glauco Souza
- Torsten Binder



- Alexandra Oertel
- Beat Bornhauser



Come to see us at **booth #1037**





Tecan – Who we are

At Tecan we are driven to improve people’s lives and health. We do this by empowering our customers to scale healthcare innovation globally from life science to the clinic. Tecan is a pioneer and global leader in laboratory automation. As an original equipment manufacturer (OEM), Tecan is also a leader in developing and manufacturing OEM instruments, components and medical devices that are then distributed by partner companies. Founded in Switzerland in 1980, the company has more than 3,300 employees, with manufacturing, research and development sites in Europe, North America and Asia, and maintains a sales and service network in over 70 countries. Registered shares of Tecan Group are traded on the SIX Swiss Exchange (TECN; ISIN CH0012100191).

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A high-angle, top-down view of a large crowd of people, each wearing a different colored shirt, forming the shape of a world map. The map is centered on the Atlantic Ocean, with North and South America on the left and Europe, Africa, and Asia on the right. The text "Scaling healthcare innovation globally." is overlaid in a black serif font across the center of the map. At the bottom of the image, there is a horizontal line of small, colorful vertical bars in various colors (red, orange, yellow, green, blue, purple, pink, etc.).

Scaling healthcare innovation globally.

Literature magnetic 3D Bioprinting

- ★ *Nature Nanotechnology* (2010)
- ★ *Neoplasia* (2010)
- ★ *Atherosclerosis* (2012)
- ★ *Tissue Engineering Part C: Methods* (2012)
- ★ *Nature* (2013) - Cell culture: A better brew
- ★ *Nature Reviews Cancer* (2013)
- ★ *Tissue Engineering Part C: Methods* (2013)
- ★ *Biochimica et Biophysica Acta* (2013)
- ★ *Acta Biomaterialia* (2013)
- ★ *Scientific Reports* (2013)
- ★ *Nature Protocols* (2013)
- ★ *Scientific Reports* (2014)
- ★ *Scientific Reports* (2015)
- ★ *AIMS Biengineering* (2016)
- ★ *Scientific Reports* (2016)
- ★ *Oncotarget* (2016)
- ★ *Int. J. Mol. Sci.* (2017)
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- ★ *SLAS Discovery* (2018)
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- ★ *Biomaterials* (2018)
- ★ *Tissue Engineering* (2019)
- ★ *Biofabrication* (2019)
- ★ *Scientific Reports* (2019)
- ★ *Cells* (2020)

